IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Meissner et al.

Serial Number: 09/393,023 — Group Art Unit: 1646

Filed: September 9, 1999 — Examiner: Kaufman, C.

For: Human Criptin Growth Factor — Attorney Docket: PF200D1

PETITION UNDER 37 C.F.R. §§ 1.144 and 1.181(c)

#19

John Doll
Director: Technology Group 1600
Washington, D.C. 20231

Sir:

Applicants hereby petition under 37 C.F.R. §§ 1.144 and 1.181(c) the final restriction requirement (Paper No.17) mailed on November 26, 2001. Applicants submit concurrently herewith: a copy of the originally filed claims (Exhibit A); a copy of the initial restriction requirement, Paper No.8 (Exhibit B); a copy of Applicants' provisional election with traverse and amendment (Exhibit C); a copy of the further restriction requirement, Paper No.12 (Exhibit D); a copy of Applicants' response to the further restriction requirement and provisional election with traverse (Exhibit E); a copy of the final restriction requirement, Paper No.17 (Exhibit F); and a copy of the Federal Register: June 15, 1998, Vol. 63, No. 114, pages 32639-32644 (Exhibit G). No fee is believed due in connection with the filing of this petition, but in the event a fee is required, please charge the fees to our Deposit Account No. 08-3425.

I. Background

A. On September 9, 1999, Applicants filed the above-captioned application, which included claims 1-20. The originally submitted claims are shown in Exhibit A.

B. On December 13, 2000, a restriction requirement was mailed, Paper No.8 (Exhibit B), to Applicants indicating that restriction of the claims is required under 35 U.S.C. § 121 because the "inventions are distinct...and have acquired a separate status in the art." *See*, Paper No.8, page 4, third paragraph.

C. On May 17, 2001, Applicants submitted a provisional election with traverse and amendment under 37 C.F.R. § 1.143 (Exhibit C). In their response, Applicants traversed the restriction requirement under 37 C.F.R. § 1.143, giving reasons why the restriction was

improper. In addition, Applicants provisionally elected the inventions of Group I, drawn to polypeptides (as set out by the Examiner in Paper No.8). Applicants also canceled claims 14-15 and added new claims 21-95 directed to subject matter falling within the scope of Group I, as defined by the Examiner.

D. On July 6, 2001, the Examiner mailed Paper No.12 (Exhibit D). In Paper No.12, the Examiner acknowledged Applicants' election with traverse of Group I (represented by claims 21-95). *See* Paper No.12, page 2, first paragraph. Upon reconsideration, the Examiner deemed the restriction between the groups proper. *See, Id.* In addition, the Examiner stated in Paper No.12, second paragraph (emphasis in original):

> Applicants' newly filed claims are drawn to numerous patentably distinct protein sequences and a method of producing the protein. Thus, further restriction *within* the formerly presented Group I is required, as follows:
>
> The claims are drawn to numerous patentably distinct proteins, each of which constitutes a patentably distinct product. Applicants are required to elect a single invention of a protein, selected from the group consisting of: a protein comprising a polypeptide selected from the group consisting of the following regions of SEQ ID NO:2: Residues 1-223, 1-173, 24-223, 24-67, 24-173, 45-128, 68-173, 68-223, 129-207 and 174-223 (including polypeptides $\geq$ 90% identical; i.e. elect one from the previous Markush group), and a single ultimate species of a fragment of residues 1-223 which retains function (as in claim 21(k)), and a fragment of $\geq$ 30 amino acids of SEQ ID NO:2.

E. On September 5, 2001, Applicants submitted a response to the second restriction requirement imposed by the Examiner (Exhibit E). In their response, Applicants traversed the restriction requirement under 37 C.F.R. § 1.143, giving reasons why the restriction was improper, requested that the restriction be withdrawn, and provisionally elected claim 21(e) as required by 37 C.F.R. § 1.143. Applicants also reserved their right to petition. *See*, Exhibit E, page 2, first full paragraph.

F. On November 26, 2001, the Examiner mailed Paper No.17 (Exhibit F). The Examiner acknowledged Applicants' traversal (*see* Exhibit F, page 2, paragraph 2) and reconsidered the restriction requirement. After reconsidering the restriction requirement, the Examiner concluded that the "restriction is still deemed proper and is therefore made final." *See* Exhibit F, page 2, paragraph 5.

G. Applicants hereby petition the final requirement for restriction (Paper No.17) under 37 C.F.R. §§ 1.144 and 1.181(c). The instant petition was deferred until the current time, but is nonetheless timely filed under 37 C.F.R. § 1.144.

H. Applicants present the following reasons why the Examiner's restriction requirement is improper:

1. The Examiner failed to consider whether the claimed inventions were "independent" as required by the plain and unambiguous meaning of the applicable statute, 35 U.S.C. § 121.
2. The Examiner improperly concluded that the separately claimed inventions are "distinct."

II. The Examiner failed to consider whether the claimed inventions were "independent" as required by the plain and unambiguous meaning of the applicable statute, 35 U.S.C. § 121

The Examiner has cited 35 U.S.C. § 121 as authority in requiring restriction of claims 21-95. Applicants contend that the Examiner improperly exercised her discretion in requiring restriction of the claimed inventions. The Examiner's action is not consistent with the plain and unambiguous meaning of the applicable statute, 35 U.S.C. § 121. The first clause of 35 U.S.C. § 121 reads as follows (emphasis added):

> If two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the inventions.

The statute unambiguously requires that two or more inventions claimed in one application be both independent and distinct before the Director may exercise his discretion in requiring the application to be restricted to one of the inventions. Thus, the Examiner (acting under the Director) must satisfy a two-prong analysis before her discretion requiring restriction may be invoked. First, the Examiner must conclude that the claimed inventions are "independent," and second, the Examiner must conclude that the inventions are "distinct." It is clear from the statute that the term "independent" and the term "distinct" are not one in the same. As conceded in the M.P.E.P:

> 'Independent', of course, means not dependent. If 'distinct' means the same thing, then its use in the statute and the rule is redundant. M.P.E.P. § 802.01 at 800-3.

Further, the M.P.E.P. defines the term "independent" as follows:

> [t]he term 'independent' (i.e., not dependent) means that there is no disclosed relationship between the two or more subjects disclosed, that is, they are unconnected in design, operation, or effect... M.P.E.P. § 802.01 at 800-3.

Claims 21(b)-(k), 46(a)-(k), and 84, and the claims dependent therefrom, hereinafter "the fragment and variant claims," are clearly not "independent" from claims 21(a), 22, and the

claims dependent therefrom, hereinafter "the full-length claims," as defined in M.P.E.P. § 802.01. The polypeptides of the fragment and variant claims are related to the polypeptide of the full-length claims in that they are connected in structure (i.e., "design"). For example, the sequence of a polypeptide fragment is related to the full-length sequence in that the sequence of a fragment is contained within the full-length sequence. Likewise, the sequence of a variant polypeptide is related to the full-length sequence by virtue of containing a specified range of identical amino acids with respect to the full-length sequence. Thus, the claimed polypeptides have a structural relationship, connected in design, and, therefore, are "dependent" as defined in M.P.E.P. § 802.01.

While the Examiner concluded that the claimed inventions are "distinct" and consequently required restriction under 35 U.S.C. § 121 (*See* Exhibits D and F), the Examiner did not determine whether the claimed inventions were "independent." In failing to do so, the Examiner improperly exercised her discretion because she did not first conclude that the inventions were "independent and distinct," as required by the statute. Moreover, Applicants contend that the claimed inventions are related, i.e., not "independent," therefore, discretionary restriction of claims 21-95 cannot be proper. Accordingly, Applicants respectfully request that the restriction requirement be withdrawn and that the restricted claims be rejoined and examined together.

III. The Examiner improperly concluded that the separately claimed polypeptides are "distinct"

As stated above, 35 U.S.C. § 121 requires that two or more inventions claimed in one application be both independent and distinct before an Examiner may exercise her discretion in requiring restriction to one of the inventions. Applicants submit that, even in the event that the statute recited, "independent or distinct inventions," rather than "independent and distinct inventions," the Examiner's restriction would remain improper because the claimed inventions are not "distinct" as defined in M.P.E.P. § 802.01. M.P.E.P. § 802.01 reads as follows (emphasis in original):

> The term 'distinct' means that two or more subjects as disclosed are related, for example, as combination and part (subcombination) thereof, process and apparatus for its practice, process and product made, etc., but are capable of separate manufacture, use, or sale as claimed, AND ARE PATENTABLE (novel and unobvious) OVER EACH OTHER (though they may each be unpatentable over the prior art). It will be noted that in this definition the term related is used as an alternative for dependent in referring to subjects other than independent subjects.

Thus, combination and subcombination claims are "distinct" when they are patentable over one another.

The M.P.E.P. defines a combination as "an organization of which a subcombination or element is a part." M.P.E.P. § 806.05(a). The USPTO has previously applied this combination-subcombination analysis to biological sequences. *See*, e.g., Exhibit G, page 32640, third column, second full paragraph to page 32641, second paragraph. Here, the USPTO has characterized a large polynucleotide sequence as a combination and a fragment of the large sequence as a subcombination. Specifically, the USPTO states:

> [a] claim such as 'A gene comprising SEQ ID NO:1,' can be viewed as a species claim in which the preamble recites a combination and the body of the claim recites a subcombination: The 'gene' is the combination and 'SEQ ID NO:1' (which is a fragment of the gene) is the subcombination....
>
> Likewise, generic claims to sequences can be viewed as a genus of such combination-subcombination claims. For example, a claim such as 'A nucleic acid comprising SEQ ID NO:1' can be viewed as a genus claim in which each member of the genus (each species) is itself a combination-subcombination: Each member of the genus 'nucleic acid' is a combination containing the subcombination of 'SEQ ID NO:1' (which is a fragment of the nucleic acid). Federal Register, June 15, 1998, Volume 63, No. 114, page 32640, third column, last paragraph to page 32641, second paragraph.

Thus, fragments of a sequence are a subcombination of a larger sequence (combination). Following this analysis, claims to the full-length polypeptide sequence are claims to a combination and claims to fragments or variants of the full-length polypeptide sequence (i.e., the combination) are subcombination claims.

<u>In order to establish that combination and subcombination inventions are distinct, two-way distinctness must be shown</u>

M.P.E.P. § 806.05(c) sets forth the criteria of distinctness for combination and subcombination claims. M.P.E.P. § 806.05(c) reads:

> [i]n order to establish that combination and subcombination inventions are distinct, two-way distinctness must be shown.

Therefore, to establish distinctness of the instant combination and subcombination inventions, the Examiner must show that two-way distinctness exists between the full-length sequence (the combination) and the fragments and variants of the sequence (the subcombinations).

The full-length claims and the fragment and variant claims are not "two-way" distinct

The full-length claims and the fragment and variant claims are not "two-way" distinct. For example, if the polypeptide of the full-length claims (i.e., the combination) was known in the art before the invention of the polypeptides of the fragment and variant claims (the subcombination claims), the subcombinations would not be patentable as claimed. This is because the full-length sequence would anticipate the fragment and variant claims. Thus, the Examiner erred in concluding that claims 21-95 are patentably distinct.

IV. Conclusion

In light of the above, the final restriction requirement imposed by the Examiner in Paper No.17 (Exhibit F) was improper. First, the Examiner failed to consider whether the claimed inventions were "independent" as required by the plain and unambiguous meaning of the applicable statute, 35 U.S.C. § 121. Second, the Examiner erred in concluding that the separately claimed inventions are "distinct." Therefore, Applicants respectfully petition the Director for the withdrawal of the restriction requirement. No fee is believed due in connection with the filing of this petition, but in the event a fee is required, please charge the fees to our Deposit Account No. 08-3425.

Respectfully submitted,

Dated: March 27, 2002

Charles E. Van Horn #40266

for Michele M. Wales (Reg. No. 43,975)
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MMW/SA

[redacted]

EXHIBIT A

WHAT IS CLAIMED IS:

1. An isolated polynucleotide comprising a member selected from the group consisting of:

(a) a polynucleotide encoding the polypeptide comprising amino acid -23 to amino acid 207 as set forth in Figure 1;

(b) a polynucleotide encoding the polypeptide comprising amino acid 1 to amino acid 207 as set forth in Figure 1;

(c) a polynucleotide encoding the polypeptide comprising amino acid 1 to amino acid 150 as set forth in Figure 1;

(d) a polynucleotide encoding the polypeptide comprising amino acid 45 to amino acid 150 as set forth in Figure 1;

(e) a polynucleotide capable of hybridizing to and which is at least 70% identical to the polynucleotide of (a), (b), (c) or (d); and

(f) a polynucleotide fragment of the polynucleotide of (a), (b), (c), (d) or (e).

2. The polynucleotide of Claim 1 wherein the polynucleotide is DNA.

3. An isolated polynucleotide comprising a member selected from the group consisting of:

(a) a polynucleotide which encodes a mature polypeptide encoded by the DNA contained in ATCC Deposit No. 97142;

(b) a polynucleotide which encodes a polypeptide expressed by the DNA contained in ATCC Deposit No. 97142;

(c) a polynucleotide capable of hybridizing to and which is at least 70% identical to the polynucleotide of (a) or (b); and

(c) a polynucleotide fragment of the polynucleotide of (a), (b) or (c).

4. The polynucleotide of claim 2 comprising the sequence as set forth in Figure 1 from nucleotide 1 to nucleotide 771.

5. The polynucleotide of claim 2 comprising the sequence as set forth in Figure 1 from nucleotide 62 to nucleotide 771.

6. The polynucleotide of claim 2 comprising the sequence as set forth in Figure 1 from nucleotide 151 to nucleotide 771.

7. The polynucleotide of claim 2 comprising the sequence as set forth in Figure 1 from nucleotide 283 to nucleotide 600.

8. A vector containing the DNA of Claim 2.

9. A host cell genetically engineered with the vector of Claim 8.

10. A process for producing a polypeptide comprising: expressing from the host cell of Claim 9 the polypeptide encoded by said DNA.

11. A process for producing cells capable of expressing polypeptide comprising genetically engineering cells with the vector of Claim 8.

12. A polypeptide comprising a member selected from the group consisting of (i) a polypeptide having the deduced amino acid sequence of Figure 1 and fragments,

analogs and derivatives thereof; and (ii) a polypeptide encoded by the cDNA of ATCC Deposit No. 97142 and fragments, analogs and derivatives of said polypeptide.

13. A compound which activates a receptor for the polypeptide of claim 12.

14. A compound which inhibits the the polypeptide of claim 12.

15. An antibody against the polypeptide of claim 12.

16. A process for identifying compounds which inhibit activation of the polypeptide of claim 12 comprising:

contacting cells which express a CGF receptor on the surface thereof with labeled CGF and a compound to be screened under conditions suitable for binding of ligands to said receptor; and

determining the extent of binding of labeled CGF to the receptor by measuring the amount of label attached to the receptor.

17. A process for identifying compounds which inhibit activation of the polypeptide of claim 12 comprising:

contacting cells which express a CGF receptor on the surface thereof with a compound to be screened under conditions suitable for binding of ligands to said receptor; and

determining the extent of binding of of the compound to the receptor and the lack of a signal generated by the binding.

18. A process for identifying compounds which activate a receptor to the polypeptide of claim 12 comprising:

contacting cells which express a CGF receptor on the surface thereof with a compound to be screened under conditions suitable for binding of ligands to said receptor; and

determining the extent of binding of the compound to the receptor and the presence of a signal generated by the binding.

19. A process for diagnosing a disease or a susceptibility to a disease related to a mutation in the polynucleotide of claim 1 comprising:

determining a mutation in the polynucleotide of claim 1.

20. A diagnostic process comprising:

analyzing for the presence of the polypeptide of claim 12 in a sample derived from a host.

[redacted]

EXHIBIT B

[redacted]

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/393,023	09/09/99	MEISSNER	P PF-200

HM22/1213

MICHELLE S. MARKS
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9410 KEY WEST AVENUE
ROCKVILLE MD 20850

EXAMINER	
KAUFMAN, C	
ART UNIT	PAPER NUMBER
1646	8

DATE MAILED: 12/13/00

RECEIVED
DEC 15 2000
HGS PATENT DEPT.

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/393,023	MEISSNER ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 1999* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-13, drawn to polynucleotide, vector, host cell, method of producing modified cell, method of producing polypeptide, polypeptide, and agonist, classified in Class 435, subclasses 69.1.

II. Claim 14 and 15, drawn to antagonist and antibody, classified in Class 530, subclass 388.24.

III. Claims 16-18, drawn to process for identifying agonist or antagonist with binding assay, classified in Class 435, subclass 7.21.

IV. Claim 19, drawn to method of diagnosing by mutation analysis, classified in Class 435, subclass 6.

V. Claim 20, drawn to method of detecting polypeptide presence, classified in Class 435, subclass 7.1, for example (classification dependent on method steps).

The inventions are distinct, each from the other because of the following reasons:

The protein of Group I is related to the antibody of Group II by virtue of being the cognate antigen, necessary for the production of the antibodies. Although the protein and antibody are related due to the necessary stearic complementarity of the two, they are distinct inventions because the protein can be used for another and materially different process other than for production of the antibody, such as to assay or purify the natural receptor for the protein or in assays for the identification of agonist or antagonists of the receptor protein. The methods of Group I are unrelated to the antibody of Group II because the antibody is not required for the methods and can be used in a materially different process such as immunoprecipitation. The nucleic acid encodes the protein, but cannot itself be used to make the antibody or antagonist. The protein is related to the antagonist because they interact, however, they are necessarily structurally and functionally distinct.

Groups I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product

as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the protein of Group I which is required for the assays of Group III can be used for a materially different process such as in performing as an antigen in the making of an antibody or in isolation of its native receptor. Additionally, the methods of Group I are distinct from those of Group III because they have materially different steps and purposes/endpoints. The nucleic acid cannot be used in the methods of Group III.

The nucleic acid of Group I and method of Group IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the nucleic acid of Group I can be used for a materially different process such as for screening a cDNA library to isolate species homologues or to produce the encoded protein. The methods of Groups I and IV are distinct because they are unrelated in process steps and function/use.

The products of Group I are unrelated to the method of Group V in that the agonist or nucleic acid of Group I is not required for the detection of the protein in a sample from a host. This process maybe practiced with antibodies to the protein. Additionally, the agonist or nucleic acid may be used for materially different processes such as agonist activation of the receptor or nucleic acid blotting (*e.g.*, Southern blotting). The methods of Groups I and V are distinct because the methods of Group I do not require components that can be used in that of Group V (e.g. antibodies or sample from host). They also have materially different process steps.

Group II is unrelated to and distinct from Groups III and IV. The antibody of Group II is not required for the processes of Groups III and IV. Additionally the antibody may be used for materially different processes such as for immunoaffinity purification of its antigen or for immunocytochemistry to identify protein presence in specific tissues.

The products of Groups II and processes of Group V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the antibody of Group II may be

used for another materially different process such as to purify the polypeptide. Additionally, the process of Group V can be practiced with another materially different product, such as with its native receptor.

Groups III-V are unrelated processes that are functionally distinct and may be practiced in different manners, and if determined to be patentable, would also be patentably distinct with one not required for the other. The process for identifying agonists and antagonist of Group III does not require either DNA or antibodies, but does require the CGF receptor. The method of Group IV for diagnosing through mutation analysis requires polynucleotides but not antibodies or the receptor. The method of Group V of detecting polypeptide presence from a cell sample can be practiced with the antibody but not DNA, nor does it require that the receptor be present.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and the search required for one group is not coextensive with any other, restriction for examination purposes as indicated is proper.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

December 12, 2000

[redacted]

EXHIBIT C

VIA HAND DELIVERY MAY 17, 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Meissner et al.

Application Number: 09/393,023 Group Art Unit: 1646

Filed: September 9, 1999 Examiner: Kaufman, C.

Title: Human Criptin Growth Factor Attny. Docket No.: PF200D1

PROVISIONAL ELECTION UNDER 37 C.F.R. § 1.143
WITH TRAVERSE AND AMENDMENT UNDER 37 C.F.R. § 1.111

Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action dated December 13, 2000, Applicants provisionally elect, *with traverse*, Group I represented by newly added claims 21 to 95, for further prosecution. Applicants reserve the right to file one or more divisional applications directed to the non-elected inventions should the restriction requirement be made final. Applicants submit concurrently herewith: (a) a Supplemental Information Disclosure Statement, Form PTO/SB/08, and copies of references AG to AK; (b) a Petition for an Extension of Time for five (5) months, up to and including May 17, 2001; (c) a Fee Transmittal Sheet; and (d) a copy of the Second Preliminary Amendment submitted on December 8, 1999 and the returned date stamped postcard. Please amend the application as follows.

Amendments

In the Specification:

On page 1, please delete the first paragraph after the title, which begins "This application is a Divisional . . . ." and replace it with:

-- This application is a Divisional of U.S. Application No. 08/471,371 filed June 6, 1995, now U.S. Patent 5,981,215 issued November 9, 1999.--

Please delete the fourth paragraph on page 4, which begins "A polynucleotide encoding a polypeptide of the present invention . . ." and ends " . . .has conserved cysteine residues in common with cripto growth factor," and replace it with:

--A polynucleotide encoding a polypeptide of the present invention was discovered in a cDNA library derived from human pancreatic cancer tissue. It is structurally related to the human cripto growth factor. It contains an open reading frame encoding a protein of 223 amino acid residues of which approximately the first 23 amino acids residues are the putative leader sequence such that the mature protein comprises 200 amino acids. As shown in figure 2 the polypeptide of the present invention has conserved cysteine residues in common with cripto growth factor.--

In the Claims:

Please cancel claims 1-13, 15, and 17-18 without prejudice.

Please add the following new claims:

--21. (New) An isolated protein comprising a polypeptide having an amino acid sequence selected from the group consisting of:

(a) amino acid residues 1 to 223 of SEQ ID NO:2;

(b) amino acid residues 1 to 173 of SEQ ID NO:2;

(c) amino acid residues 24 to 223 of SEQ ID NO:2;

(d) amino acid residues 24 to 67 of SEQ ID NO:2;

(e) amino acid residues 24 to 173 of SEQ ID NO:2;

(f) amino acid residues 45 to 128 of SEQ ID NO:2;

(g) amino acid residues 68 to 173 of SEQ ID NO:2;

(h) amino acid residues 68 to 223 of SEQ ID NO:2;

(i) amino acid residues 129 to 207 of SEQ ID NO:2;

(j) amino acid residues 174 to 223 of SEQ ID NO:2; and

(k) a polypeptide fragment of amino acids 1 to 223 of SEQ IDNO:2 wherein said polypeptide fragment stimulates cell growth.

22. (New) An isolated protein of claim 21 which comprises amino acid residues 1 to 223 of SEQ ID NO:2.

23. (New) The isolated protein of claim 21 which comprises amino acid residues 1 to 173 of SEQ ID NO:2.

24. (New) The isolated protein of claim 21 which comprises amino acid residues 24 to 223 of SEQ ID NO:2.

25. (New) The isolated protein of claim 21 which comprises amino acid residues 24 to 67 of SEQ ID NO:2.

26. (New) The isolated protein of claim 21 which comprises amino acid residues 24 to 173 of SEQ ID NO:2.

27. (New) The isolated protein of claim 21 which comprises amino acid residues 45 to 128 of SEQ ID NO:2.

28. (New) The isolated protein of claim 21 which comprises amino acid residues 68 to 173 of SEQ ID NO:2.

29. (New) The isolated protein of claim 21 which comprises amino acid residues 68 to 223 of SEQ ID NO:2.

30. (New) The isolated protein of claim 21 which comprises amino acid residues 129 to 207 of SEQ ID NO:2.

31. (New) The isolated protein of claim 21 which comprises amino acid residues 173 to 223 of SEQ ID NO:2.

32. (New) The isolated protein of claim 21 which comprises a polypeptide fragment of amino acids 1 to 223 of SEQ ID NO:2 wherein said polypeptide fragment stimulates cell growth.

33. (New) The isolated protein of claim 21 wherein the amino acid sequence further comprises a heterologous polypeptide.

34. (New) The isolated protein of claim 24, wherein the amino acid sequence further comprises a heterologous polypeptide.

35. (New) The protein of claim 21, wherein said isolated protein is glycosylated.

36. (New) A composition comprising the isolated protein of claim 21 and a pharmaceutically acceptable carrier.

37. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the isolated protein of claim 21; and

(b) recovering the protein.

38. (New) An isolated protein comprising an amino acid sequence selected from the group consisting of:

(a) the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142;

(b) the mature form of the polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142; and

(c) a polypeptide fragment of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142 wherein said polypeptide fragment stimulates cell growth.

39. (New) The protein of claim 38 which comprises the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

40. (New) The protein of claim 38 which comprises the mature form of the polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

41. (New) The protein of claim 38 which comprises a polypeptide fragment of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142 wherein said polypeptide fragment stimulates cell growth.

42. (New) The isolated protein of claim 38 wherein the amino acid sequence further comprises a heterologous polypeptide.

43. (New) The isolated protein of claim 38, wherein said protein is glycosylated.

44. (New) A composition comprising the protein of claim 38 and a pharmaceutically acceptable carrier.

45. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the protein of claim 38; and

(b) recovering the protein.

46. (New) An isolated protein comprising an amino acid sequence 90% or more identical to an amino acid sequence selected from the group consisting of:

(a) amino acid residues 1 to 223 of SEQ ID NO:2;

(b) amino acid residues 1 to 173 of SEQ ID NO:2;

(c) amino acid residues 24 to 223 of SEQ ID NO:2;

(d) amino acid residues 24 to 67 of SEQ ID NO:2;

(e) amino acid residues 24 to 173 of SEQ ID NO:2;

(f) amino acid residues 45 to 128 of SEQ ID NO:2;

(g) amino acid residues 68 to 173 of SEQ ID NO:2;

(h) amino acid residues 68 to 223 of SEQ ID NO:2;

(i) amino acid residues 129 to 207 of SEQ ID NO:2;

(j) amino acid residues 173 to 223 of SEQ ID NO:2; and

(k) a polypeptide fragment of amino acids 1 to 223 of SEQ ID NO:2 wherein said polypeptide fragment stimulates cell growth.

47. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 1 to 223 of SEQ ID NO:2.

48. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 1 to 173 of SEQ ID NO:2.

49. (New) The isolated polypeptide of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 24 to 223 of SEQ ID NO:2.

50. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 24 to 67 of SEQ ID NO:2.

51. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 24 to 173 of SEQ ID NO:2.

52. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 45 to 128 of SEQ ID NO:2.

53. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 68 to 173 of SEQ ID NO:2.

54. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 68 to 223 of SEQ ID NO:2.

55. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 129 to 207 of SEQ ID NO:2.

56. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 173 to 223 of SEQ ID NO:2.

57. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to a polypeptide fragment of amino acids 1 to 223 of SEQ ID NO:2 wherein said polypeptide fragment stimulates cell growth.

58. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 1 to 223 of SEQ ID NO:2.

59. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 1 to 173 of SEQ ID NO:2.

60. (New) The isolated polypeptide of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 24 to 223 of SEQ ID NO:2.

61. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 24 to 67 of SEQ ID NO:2.

62. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 24 to 173 of SEQ ID NO:2.

63. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 45 to 128 of SEQ ID NO:2.

64. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 68 to 173 of SEQ ID NO:2.

65. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 68 to 223 of SEQ ID NO:2.

66. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 129 to 207 of SEQ ID NO:2.

67. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 173 to 223 of SEQ ID NO:2.

68. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to a polypeptide fragment of amino acids 1 to 223 of SEQ ID NO:2 wherein said polypeptide fragment stimulates cell growth.

69. (New) The isolated protein of claim 46 wherein the amino acid sequence further comprises a heterologous polypeptide.

70. (New) The isolated protein of claim 46, wherein said isolated protein is glycosylated.

71. (New) A composition comprising the isolated protein of claim 46 and a pharmaceutically acceptable carrier.

72. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the protein of claim 46; and

(b) recovering the protein.

73. (New) An isolated protein comprising an amino acid sequence 90% or more identical to an amino acid sequence selected from the group consisting of:

(a) the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142;

(b) the mature form of the polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142; and

(c) a polypeptide fragment of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142 wherein said polypeptide fragment stimulates cell growth.

74. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 90% or more identical to the amino acid sequence of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

75. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 90% or more identical to the amino acid sequence of the mature form of the polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

76. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 90% or more identical to the amino acid sequence of a polypeptide fragment of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142 wherein said polypeptide fragment stimulates cell growth.

77. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 95% or more identical to the amino acid sequence of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

78. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 95% or more identical to to the amino acid sequence of the mature form of the polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

79. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 95% or more identical to the amino acid sequence of a polypeptide fragment of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142 wherein said polypeptide fragment stimulates cell growth.

80. (New) The isolated protein of claim 73 wherein the amino acid sequence further comprises a heterologous polypeptide.

81. (New) The isolated protein of claim 73 wherein said isolated protein is glycosylated.

82. (New) A composition comprising the isolated protein of claim 73 and a pharmaceutically acceptable carrier.

83. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the isolated

protein of claim 73; and

(b) recovering the protein.

84. (New) An isolated protein comprising at least 30 contiguous amino acids of SEQ ID NO:2.

85. (New) The isolated protein of claim 84 further comprising at least 50 contiguous amino acids of SEQ ID NO:2.

86. (New) The isolated protein of claim 84 wherein the amino acid sequence further comprises a heterologous polypeptide.

87. (New) The isolated protein of claim 84 wherein said isolated protein is glycosylated.

88. (New) A composition comprising the isolated protein of claim 84 and a pharmaceutically acceptable carrier.

89. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the isolated protein of claim 84; and

(b) recovering the protein.

90. (New) An isolated protein comprising at least 30 contiguous amino acids of the polypeptide encoded by the cDNA contained in ATCC Deposit No. 97142.

91. (New) The isolated protein of claim 90 further comprising at least 50 contiguous amino acids of the polypeptide encoded by the cDNA contained in ATCC Deposit No. 97142.

92. (New) The isolated protein of claim 90 wherein the amino acid sequence further comprises a heterologous polypeptide.

93. (New) The isolated protein of claim 90 wherein said isolated protein is glycosylated.

94. (New) A composition comprising the isolated protein of claim 90 and a pharmaceutically acceptable carrier.

95. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the isolated protein of claim 90; and

(b) recovering the protein.--

Remarks

Claims 14, 16, 19-20 and new claims 21-95 are pending in the instant application.

Claims 1-13, 15, and 17-18 have been canceled, and new claims 21 to 95 have been added to more particularly point out and distinctly claim the subject matter Applicants regard as the invention. Support for the newly added claims is found throughout the specification as filed. Particularly, support for claims 21-32 and 38-41 can be found, for example, at page 4, lines 9-28; page 18, lines 18-31; page 43, original claim 1 and 3; and Figure 1. Support for claims 33-34, 42, 69, 80, 86, and 92 can be found, for example, at page 9, line 20 through page 10, line 4. Moreover, support for claims 35, 43, 70, 81, 87, and 93 can be found, for example, at page 17, lines 11-15, and support for claims 36, 44, 71, 82, 88, and 94 can be found, for example, at page 22, lines 13-21. Claims 37, 45, 72, 83, 89, and 95 find support, for example, at page 11, lines 12-13. Finally, support for claims 46-68, 73-79, 84-85, and 90-91 can be found, for example, at page 4, lines 9-28; page 9, line 20 through page 10, line 30; page 18, lines 5-6; page 43, original claim 1; and Figure 1.

No new matter has been added by way of this amendment. Entry of the amendment and remarks is respectfully requested.

Applicants wish to point out that a Second Preliminary Amendment was filed by Applicants on December 8, 1999 (*see, e.g.,* the attached copy of the Second Preliminary Amendment and the date stamped postcard showing receipt by the Patent Office). The Official Action of December 13, 2000 did not reflect the entry of this amendment. Applicants respectfully request that this amendment be made of record in the captioned application. Applicants note that some of the amendments to the specification which were requested in Applicants' Second Preliminary Amendment of December 8, 1999 (e.g., changes at page 4, line 18; page 4, line 20; and page 4, line 26), showed the incorrect line numbers on page 4, and in some instances showed an incorrect length of amino acid residues. Therefore, Applicants have provided a clean version and a marked up version of the changes to the specification correctly reflecting these amendments.

The Restriction Requirement

The Examiner contends that the inventions are distinct, each from the other, and thus, has required an election under 35 U.S.C. § 121.

In order to be fully responsive, Applicants hereby provisionally elect the invention of Group I, drawn to polypeptides, with traversal. Applicants point out that the claims 14-15 have been cancelled and that new claims 21 to 95 are directed to subject matter falling within the scope of Group I as defined by the Examiner.

With respect to the Examiner's division of the invention into five (5) groups and the reasons stated therefor, Applicants respectfully traverse. Applicants submit that even where two patentably distinct inventions appear in a single application, restriction remains improper unless it can be shown that the search and examination of both groups would entail a "serious burden" (*See* M.P.E.P. § 803). In the present situation, no such showing has been made.

Even assuming, *arguendo,* that Groups I-V represent distinct or independent inventions, Applicants submit that to search and examine the subject matter of all the Groups

together would not be a serious burden on the Examiner. For example, as stated by the Examiner in the Office Action dated December 13, 2000, the protein of Group I is related to the antibody of Group II. Thus, Applicants submit that a search of the polypeptide claims would clearly provide useful information for the polynucleotide claims and antibody claims. In many, if not most publications, where a published polypeptide is described, the authors also include, as a matter of routine, a polynucleotide sequence encoding this polypeptide. Thus, Applicants submit that a search of antibody claims of the invention would provide useful information for examining claims directed to both polypeptides and the polynucleotides encoding these polypeptides. Further, Applicants point out that, in many if not most publications, where a published nucleotide sequence is an open reading frame, the authors also include, as a matter of routine, the deduced amino acid sequence of the encoded polypeptide.

Similarly, a search of the polypeptide claims of the invention would clearly provide useful information for the examination of claims directed to antibodies either produced in response to or having affinity for the subject polypeptides. This is because antibodies are frequently defined by the antigens that they are produced in response to and the epitopes to which they bind. Moreover, in many publications where an antibody is described, the antigen that it was produced in response to is also described.

Further, searches of publications directed to polypeptides and the use of those polypeptides would clearly be overlapping. This is so because in many, if not most, publications which describe polypeptides, these molecules are described by their function. Thus, a search of polypeptide claims would also provide the Examiner with art directed to the manner in which the claimed polypeptides could be used to in diagnostics, identification of agonists and antagonist of the polypeptides, and/or to treat disease states.

Accordingly, Applicants respectfully request that the restriction requirement under 35 U.S.C § 121 be reconsidered and withdrawn and the instant claims be examined in one application.

Applicants retain the right to petition from the restriction requirement under 37 C.F.R. § 1.144.

Applicants respectfully request that the above-made amendments and remarks be entered and made of record in the file history of the instant application. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: May 18, 2001

Michele M. Wales (Reg. No. 43,975)
Attorney for Applicants

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Rockville, MD 20850
Phone: (301) 610-5772
Fax: (301) 309-8439

MMW/CCB/ba

[redacted]

EXHIBIT D

[redacted]

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/393,023	09/09/99	MEISSNER	P PF-200

022195
HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE MD 20850

HM12/0706

RECEIVED
JUL 09 2001
HGS PATENT DEPT.

EXAMINER	
KAUFMAN, C	
ART UNIT	PAPER NUMBER
1646	19

DATE MAILED: 07/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

[redacted]

Office Action Summary	Application No. 09/393,023	Applicant(s) MEISSNER ET AL.
	Examiner Claire M. Kaufman	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2001* .

2a)☐ This action is FINAL. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14, 16, 19-95* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *14, 16, 19-95* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Restriction Requirement:

Applicants election of Group I, now represented by claims 21-95 in paper number 10 filed 5/17/01, with traverse, is acknowledged. The traversal is on the ground(s) that the examination of the entire application would not constitute a burden to search because the Groups are related (*e.g.*, antibody to polypeptide, polypeptide to polynucleotide). This is not found persuasive because contrary to Applicants' assertion that any search of the prior art in regard to Group I will reveal whether any prior art exists as to Group II-V (claims 14, 16, 19 and 20), a search is directed to references which would render the invention obvious, as well as references directed to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter. For example, a search for the polypeptide must involve isolates produced by other than recombinant means. Also, nucleic acid references do not necessarily disclose a protein produced by tranlation of the nucleic acid. As to polypeptides and antibodies, the claimed antibodies are not required to bind only the claimed polypeptide fragment at the exclusion of other proteins. Therefore, the search for antibodies require more than searching the complete protein fragment of which it binds only a portion. For polypeptide compared to process claims, as pointed out above, a search is required for not only anticipatory references, but also those that would make obvious the invention, requiring non-coextensive searches. Therefore, restriction between groups is proper.

Applicants newly filed claims are drawn to numerous patentably distinct protein sequences and a method of producing the protein. Thus, further restriction *within* the formerly presented Group I is required, as follows:

The claims are drawn to numerous patentably distinct proteins, each of which constitutes a patentably distinct product. Applicants are required to elect a single invention of a protein, selected from the group consisting of: a protein comprising a polypeptide selected from the group consisting of the following regions of SEQ ID NO:2: Residues 1-223, 1-173, 24-223, 24-67, 24-173, 45-128, 68-173, 68-223, 129-207 and 174-223 (including polypeptides $\geq$ 90% identical; i.e. elect one from the previous Markush group), and a single ultimate species of a

fragment of residues 1-223 which retains function (as in claim 21(k)), and a fragment of ≥ 30 amino acids of SEQ ID NO: 2.

Applicants should note that in some cases multiple claims encompass one of the patentably distinct inventions set forth herein, for example it is presumed by the Examiner in setting forth this requirement that the complete protein encoded by the cDNA of ATCC deposit 97142 is SEQ ID NO: 2. To be fully responsive to this requirement, Applicants are **required** to point out which claims correspond to the elected invention.

Although the classifications for these various proteins are overlapping, for instance 530/300, each represents a patentably distinct product with distinct physical and functional characteristics. Additionally, the burden of search for the Office has increased with multiple sequences because of the rapid introduction of new sequences to public sequence databases. Further the search for more than one product would be burdensome, because some are claimed not by protein sequence, but by the sequence encoded by a nucleic acid sequence, and requires a search of the corresponding region of SEQ ID NO: 1 as well as a 'reverse translation' search of the corresponding region of SEQ ID NO: 2, such that each individual sequence requires two sequence searches which are not required for any of the other sequences; or alternatively by virtue of comprising only a small portion of a disclosed protein, which requires a separate "word search" of the protein and/or nucleic acid databases, or by claiming proteins which are not 100% identical to a disclosed protein, which requires a broader search of the protein databases. Due to the use of 'comprising' language, it cannot even be said that the search for a protein comprising amino acids 1-223 of SEQ ID NO: 2 would reveal art pertaining to, for instance, a protein *comprising* amino acids 24-67 of SEQ ID NO: 2, as the latter could be found embedded in a completely different protein. Accordingly, restriction is proper.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(i).

Conclusion

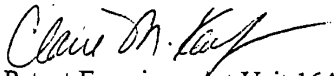
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.



Patent Examiner, Art Unit 1646

July 5, 2001

[redacted]

EXHIBIT E

VIA HAND DELIVERY SEPTEMBER 5, 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Meissner et al.

Application Number: 09/393,023 Group Art Unit: 1646

Filed: September 9, 1999 Examiner: Kaufman, C.

Title: Human Criptin Growth Factor Attny. Docket No.: PF200D1

RESPONSE TO FURTHER RESTRICTION REQUIREMENT, PROVISIONAL ELECTION, AND TRAVERSE UNDER 37 C.F.R. § 1.143

Commissioner for Patents and Trademarks
Washington, D.C. 20231

Sir or Madam:

In response to the Further Restriction Requirement mailed July 6, 2001, please enter the following provisional election, with traverse, and consider the remarks below. Applicants submit concurrently herewith: (a) a Petition for an Extension of Time for one (1) month, up to and including September 6, 2001; (b) a Fee Transmittal Sheet; and (c) Associate Power of Attorney.

Remarks

Claims 14, 16, and 19-95 are pending in the instant application.

Applicants request reconsideration and withdrawal of the present restriction requirement.

The Restriction Requirement

The Examiner appears to be requiring an election of "species" (*i.e.*, sequence) within the provisionally elected Group I.

More particularly, the Examiner alleges:

> The claims are drawn to numerous patentably distinct proteins, each of which constitutes a patentably distinct product. Applicants are required to elect a single invention of a protein, selected from the group consisting of: a protein comprising a polypeptide selected from the group consisting of the following regions of SEQ ID NO:2: Residues 1-223, 1-173, 24-223, 24-67, 24-173, 45-128, 68-173, 68-223, 129-207 and 174-223 (including polypeptides ≥ 90% identical; i.e., elect one from the previous Markush group), and a single ultimate species of a fragment of residues 1-223 which retains

function (as in claim 21(k)), and a fragment of ≥ 30 amino acids of SEQ ID NO:2.

(*See*, Paper No. 13, Pages 2-3, Paragraph 3.)

In order to be fully responsive, Applicants hereby elect, with traverse, an isolated protein comprising amino acids 24 to 173 of SEQ ID NO:2 (Claims 21(e), 26, 33, and 35-37). Applicants reserve the right to file one or more divisional applications directed to non-elected inventions should the additional restriction requirement be made final. In such a case, Applicants retain the right to petition from the additional restriction requirement under 37 C.F.R. § 1.144.

Applicants respectfully traverse and request the withdrawal of the requirement for further restriction.

As a threshold matter, Applicants point out that MPEP § 803 lists the criteria for a proper restriction requirement:

> Under the statute an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent (MPEP § 806.04 – § 806.04(i)) or distinct (MPEP § 806.05 – § 806.05(i)).
>
> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

Thus, even assuming, *arguendo*, that the sequences listed by the Examiner represent distinct or independent inventions, restriction remains improper unless it can be shown that the search and examination of these sequences would entail a "serious burden." *See* M.P.E.P. § 803. In the present situation no such showing has been made.

The Examiner has alleged that

> Although the classifications for these various proteins are overlapping, for instance 530/300, each represents a patentably distinct product with distinct physical and functional characteristics. Additionally, the burden of search for the Office has increased with multiple sequences because of the rapid introduction of new sequences to public sequence databases. Further the search of more than one product would be burdensome, because some are claimed not by protein sequence, but by the sequence encoded by a nucleic acid sequence, and requires a search of the corresponding region of SEQ ID NO:1 as well as a 'reverse translation' search of the

> corresponding region of SEQ ID NO:2, such that each individual sequence requires two sequence searches which are not required for any of the other sequences; or alternatively by virtue of comprising only a small portion of a disclosed protein, which requires a separate "word search" of the protein and/or nucleic acid databases, or by claiming proteins which are not 100% identical to a disclosed protein, which requires a broader search of the protein databases. Due to the use of 'comprising' language, it cannot even be said that the search for a protein comprising amino acids 1-223 of SEQ ID NO:2 would reveal art pertaining to, for instance, a protein *comprising* amino acids 24-67 of SEQ ID NO:2, as the latter could be found embedded in a completely different protein. Accordingly, restriction is proper.

(*See*, Paper No. 13, Page 3, Paragraph 5, emphasis in original.)

Applicants disagree and submit that an art search with a protein comprising amino acid residues 24 to 173 of SEQ ID NO:2 would be largely overlapping with that for a protein comprising amino acid residues 1-223, 1-173, 24-223, 24-67, 45-128, 68-173, 68-223, 129-207, or 174-223 of SEQ ID NO:2 (including polypeptides $\geq$ 90% identical to those fragments), a fragment of residues 1-223 which retains function, and a fragment of $\geq$ 30 amino acids of SEQ ID NO:2. Thus, the search and examination of all claims which encompass a protein comprising amino acid residues 1-223, 1-173, 24-223, 24-67, 24-173, 45-128, 68-173, 68-223, 129-207, or 174-223 of SEQ ID NO:2 (including polypeptides $\geq$ 90% identical to those fragments), a fragment of residues 1-223 which retains function, and a fragment of at least 30 contiguous amino acids of SEQ ID NO:2 would not entail a serious burden.

In addition, Applicants respectfully remind the Examiner that upon allowance of a generic claim, Applicants will be entitled to the consideration of additional "species" which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141. MPEP § 809.02(a).

Thus, Applicants respectfully request that the further restriction within the formerly presented Group I be withdrawn so the restricted subject matter can be examined together.

Applicants respectfully point out that the provisionally elected claim 21(e) is overlapping in scope to the pending claims, particularly given that all of the claims are directed to SEQ ID NO:2 (or the corresponding deposited clone). Nevertheless, to the extent that the Examiner requests that Applicants "point out which claims correspond to the elected

invention" (*see*, Paper No. 13, Page 3), Applicants point out that claims 26, 33, and 35-37 are particularly directed to the provisionally elected subject matter of claim 21(e).

Conclusion

Applicants respectfully request that the above-made remarks be entered and made of record in the file history of the instant application. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: SEPTEMBER 5, 2001

Jonathan L. Klein (Reg. No. 41,119)
Attorney for Applicants

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MMW/JKE/CCB/ba

[redacted]

EXHIBIT f

[redacted]

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/393,023	09/09/1999	PAUL S. MEISSNER	PF-200	2146

22195 7590 11/26/2001

HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE, MD 20850

RECEIVED
NOV 28 2001
TECH CENTER 1600/2900

EXAMINER	
KAUFMAN, CLAIRE M	

ART UNIT	PAPER NUMBER
1646	17

DATE MAILED: 11/26/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/393,023	MEISSNER ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09/09/99, 12/08/99, 05/17/01* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,16 and 19-95* is/are pending in the application.

4a) Of the above claim(s) *14,16,19,20,22-25,27-32,34 and 38-95* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,26,33 and 35-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *14,16 and 19-95* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 September 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2,4.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendments filed 9/9/99, 12/8/99 and 5/17/01 have been entered.

Election/Restrictions

Applicant's election with traverse of Group I of protein comprising amino acids 24-173 of SEQ ID NO:2 in Paper No. 16 is acknowledged. The traversal is on the ground(s) that 1) this should be/is a species election with additional species being examined if the first species is found allowable, 2) there is no serious burden of search for examining multiple sequences. This is not found persuasive.

With respect to Applicants' first point, although the word "species" was used in the restriction of 7/6/01, it was not a "species" restriction/election. Each embodiment set forth in the restriction is a distinct and separate invention. There is no generic claim since art against a fragment would not constitute art against the full-length protein, and the art against one fragment would not necessarily constitute art against another. As a result, only one invention will be examined: a protein comprising amino acids 24-173 of SEQ ID NO:2.

With respect to Applicants' second point, there is a serious burden of search for searching the multiple sequences/proteins claimed. Some fragments are short and need to be only 90% identical to a disclosed fragment, so the sequence could be embedded within other patentably distinct proteins. Therefore, it cannot be said that they are merely fragments of a common protein. A separate search is required for each possible fragment. Searching the full-length protein sequence will not necessarily result in the identification of art pertinent to the fragments since the USPTO search system generally has a limited number of "hits" saved and the burden of search for the Office has increased with multiple sequences because of the rapid introduction of new sequences to public sequence databases.

The requirement is still deemed proper and is therefore made FINAL.

The elected invention is a protein comprising a polypeptide having an amino acid sequence of residues 24-173 of SEQ ID NO: 2. Thus, claims 21, 26, 33 and 35-37 as they are

drawn to the elected invention are under consideration. Claims 14, 16, 19, 20, 22-25, 27-32, 34 and 38-95 are withdrawn from prosecution as being drawn to a non-elected invention.

Drawings

The corrected or substitute drawings were received on 12/8/99. These drawings are approved.

Response to Amendment

The Declaration under 37 CFR 1.132 filed 12/8/99 is sufficient to address potential issues of new matter relating to the sequence differences between this and the parent application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21, 26, 33 and 35-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 32 of U.S. Patent No. 5,981,215. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims encompass the protein encoded by the cDNA clone contained in ATCC No. 97142. Further, it would have been obvious to express the cDNA in a host cell, recovering the protein which can be glycosylated depending on the type of host cell. Such a protein is generally recovered in a buffer, a pharmaceutically acceptable carrier. It further would have been obvious for the protein to further comprise a heterologous polypeptide

which functioned as a purification tag, for example, because it was well known that the many commercially available protein purification tags were valuable tools at the time the instant invention was made (see also claim 42 and 47 of US Patent No. 5,981,215).

Claim Objections

Claims 21, 33 and 35-37 are objected to for encompassing multiple patentably distinct inventions. The claims should be amended to include only the elected invention. Correction is required.

Objections and Rejections under 35 U.S.C. §§101 and 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 21, 26, 33 and 35-37 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility.

The utility set forth in the specification p.17, last paragraph, is that of pancreatic cancer diagnosis. This is based on "An initial Northern blot analysis [that] has shown very high expression in pancreatic cancer cells." For several reasons this is not a specific or substantial utility. First, it is not know how the level of expression compares to expression in normal noncancerous cells, nor if the expression was analyzed in cell cultures or in cancerous tissue. Markers for cell lines are not necessarily representative of primary cell cultures or tissue since it is well known that cells can undergo changes in expression when cultured for extended passages. Also, a cancer cell line is representative of only a single sample (cell lines originate from 1 patient's cells), which is not enough information to conclude that protein alteration in that cell line is a universal phenomenon in all or most pancreatic cell samples. Second, polynucleotide expression is not necessarily indicative of protein expression. There is no information on altered level of protein (the claimed product) in pancreatic cancer cells.

The specification teaches that the mature criptin protein (amino acids 24-223 of SEQ ID NO:2) has the putative activity of wound healing and stimulation of vasculogenesis (p. 18,3rd and 4thfull paragraph). The prior art teaches a structurally related protein called "cripto" which has been identified as a cancer marker (p. 2, third paragraph; and references AA and AE), as well as a related gene called "CR-3" (AB), the function of which is also unknown. Neither of these prior art proteins is disclosed as having a transmembrane domain, although criptin is disclosed as having a transmembrane domain (p. 4, 8 lines from bottom). In the current instance the nature the invention is largely unknown since the related prior art proteins have no described function except as tumor cell markers and have a conserved "EGF motif" which confers some structural form. There are no examples of criptin promoting would healing or vasculogenesis. The list of tissue in which it may promote would healing is diverse: skin, bone, muscle, lung..., and no specific tissue is identified nor under what circumstances criptin can actually promote wound healing (*e.g.*, cellular state of tissue--proliferating or differentiating, effective amount, or *in vivo* compared to *in vitro* activity). Also, the currently claimed protein has several putative functions listed and a putative three dimensional structure, but without information on the relationship of structure to function.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 26, 33 and 35-37 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the means by which the protein can be produced. There s nothing to indicate the host cell anything by which it can produce the protein, for example, a nucleic acid encoding the protein.

Claim 37 is indefinite because in step (b), it is unclear if "the protein" recovered is said isolated protein of claim 21 or if it is another protein in/from the cell.

Claim 34 is indefinite for failing to indicate the relationship between the recited structural elements. Specifically, it is not clear how the "heterologous polynucleotide" of claim 34, for example, relates to the polynucleotide of claim 21. In claim 34, it is not clear whether the heterologous sequence is attached at an end or might be internally inserted.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

November 15, 2001

[redacted]

EXHIBIT 6

FOR FURTHER INFORMATION CONTACT: Dr. Subhas G. Malghan, FQA Program Manager, Building 820, Room 306, NIST, Gaithersburg, MD 20899; telephone (301) 975–5120, fax (301) 975–5414, E-mail: malghan@nist.gov.

SUPPLEMENTARY INFORMATION: On June 1, 1998, NIST announced in the **Federal Register**, (63 FR 29702), that it would be holding a public meeting on June 16, 1998, to provide details and interpretations on the regulations related to the Quality Assurance System (QAS) of fastener manufacturing contained in the April 14, 1998, final regulation under the Fastener Quality Act. NIST is postponing that meeting and will issue a future notice announcing a new date for the meeting.

Dated: June 10, 1998.

Robert E. Hebner,

Acting Deputy Director, National Institute of Standards and Technology.

[FR Doc. 98–15935 Filed 6–12–98; 8:45 am]

BILLING CODE 3510–13–M

DEPARTMENT OF COMMERCE

Patent and Trademark Office

[Docket No. 980605148–8148–01]

Request for Comments on Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶1 "Written Description" Requirement

AGENCY: Patent and Trademark Office, Commerce.

ACTION: Notice and request for public comments.

SUMMARY: The Patent and Trademark Office (PTO) requests comments from any interested member of the public on the following interim guidelines. These guidelines will be used by PTO personnel in their review of biotechnological patent applications for compliance with the "written description" requirement of 35 U.S.C. 112 ¶ 1. Although the guidelines are directed primarily to written descriptions of biotechnological inventions, they reflect the current understanding of the PTO and apply across the board to all relevant technologies.

DATES: Written comments on the interim guidelines will be accepted by the PTO until September 14, 1998.

ADDRESSES: Written comments should be addressed to Box 8, Commissioner of Patents and Trademarks, Washington, D.C. 20231, marked to the attention of Scott A. Chambers, Associate Solicitor or to Box Comments, Assistant Commissioner for Patents, Washington, D.C. 20231 marked to the attention of Linda S. Therkorn. Alternatively, comments may be submitted to Scott Chambers via facsimile at (703) 305–9373 or by electronic mail addressed to "scott.chambers@uspto.gov" or to Linda Therkorn via facsimile at (703) 305–8825 or by electronic mail addressed at "linda.therkorn@uspto.gov."

FOR FURTHER INFORMATION CONTACT: Scott Chambers by telephone at (703) 305–9035, by facsimile at (703) 305–9373, by mail to his attention addressed to Box 8, Commissioner of Patents and Trademarks, Washington, D.C. 20231, or by electronic mail at "scott.chambers@uspto.gov"; or Linda Therkorn by telephone at (703) 305–8800, by facsimile at (703) 305–8825, by mail addressed to Box Comments, Assistant Commissioner for Patents, Washington, D.C. 20231, or by electronic mail at "linda.therkorn@uspto.gov."

SUPPLEMENTARY INFORMATION: The PTO requests comments from any interested member of the public on the following interim guidelines. These guidelines will be used by PTO personnel in their review of biotechnological patent applications for compliance with the "written description" requirement of 35 U.S.C. 112 ¶ 1. Although the guidelines are directed primarily to written descriptions of biotechnological inventions, they reflect the current understanding of the PTO and apply across the board to all relevant technologies. Because these guidelines govern internal practices, they are exempt from notice and comment rulemaking under 5 U.S.C. 553(b)(A).

Written comments should include the following information: (1) name and affiliation of the individual responding; and (2) an indication of whether the comments offered represent views of the respondent's organization or are they respondent's personal views. The PTO is particularly interested in comments relating to: (1) the accuracy of the methodology; (2) relevant factors to consider in determining whether the written description requirement of 35 U.S.C. 112 ¶ 1 is satisfied; (3) whether the scope of these guidelines should be limited to certain technologies, such as biotechnology, or even a particular area of biotechnology such as nucleic acids, or encompass all technologies generally; (4) whether the scope of these guidelines should be expanded to include processes and/or product-by-process claims; and (5) the impact these guidelines may have on currently pending applications as well as future applications.

Parties presenting written comments are requested, where possible, to provide their comments in machine-readable format in addition to a paper copy. Such submissions may be provided by electronic mail messages sent over the Internet, or on a 3.5" floppy disk formatted for use in either a Macintosh, Windows, Windows for Workgroups, Windows 95, Windows NT, or MS-DOS based computer.

Written comments will be available for public inspection on or about September 14, 1998, in Suite 918, Crystal Park 2, 2121 Crystal Drive, Arlington, Virginia. In addition, comments provided in machine-readable format will be available through anonymous file transfer protocol (ftp) via the Internet (address: comments.uspto.gov) and through the World Wide Web (address: www.uspto.gov).

Interim Guidelines for the Examination of Patent Applications Under The 35 U.S.C. 112 ¶ 1 "Written Description" Requirement

These "Written Description Guidelines" are intended to assist Office personnel in the examination of patent applications for compliance with the written description requirement of 35 U.S.C. 112, ¶ 1, in view of *University of California* v. *Eli Lilly*[1] and the earlier cases *Fiers* v. *Revel*[2] and *Amgen, Inc.* v. *Chugai Pharmaceutical Co.*[3] These Interim Guidelines are directed primarily to determining whether there is written description support for product claims and are not intended to specifically address the description necessary to support process or product-by-process claims. Similarly, these Guidelines are not intended to directly address the question of new matter, which is currently addressed in the Manual of Patent Examining Procedure §§ 2163.06–.07. The Final Guidelines may address these additional issues if public comment suggests they should be addressed. These guidelines are based on the Office's current understanding of the law and are believed to be fully consistent with binding precedent of the Supreme Court, the Federal Circuit, and the Federal Circuit's predecessor courts.

These guidelines do not constitute substantive rulemaking and hence do not have the force and effect of law. They are designed to assist Office personnel in analyzing claimed subject matter for compliance with substantive law. Rejections will be based upon the substantive law, and it is these rejections which are appealable. Consequently, any failure by Office personnel to follow the guidelines is neither appealable nor petitionable.

These guidelines are intended to form part of the normal examination process. Thus, where Office personnel establish a *prima facie* case of lack of written description for a claim, a thorough review of the prior art and examination on the merits for compliance with the other statutory requirements, including those of 35 U.S.C. 101, 102, 103, and 112, is to be conducted prior to completing an Office action which includes a rejection for lack of written description.

Office personnel are to rely on these guidelines in the event of any inconsistent treatment of issues involving the written description requirement between these guidelines and any earlier guidance provided from the Office. Although these guidelines address examples principally drawn from the biotechnological arts, they are intended to be equally applicable to all fields of invention.

I. General Principles Governing Compliance with the "Written Description" Requirement for Applications

The first paragraph of 35 U.S.C. 112 requires that the "specification shall contain a written description of the invention * * *" This requirement is separate and distinct from the enablement requirement.[4] This written description requirement has several policy objectives. "[T]he "essential goal" of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed."[5] Another objective is to put the public in possession of what the applicant claims as the invention. The written description requirement prevents an applicant from claiming subject matter that was not described in the specification as filed, and the proscription against the introduction of new matter in a patent application[6] serves to prevent an applicant from adding information that goes beyond the subject matter originally filed.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.[7] This requirement of the Patent Act promotes the progress of the useful arts by ensuring that patentees adequately describe their inventions in their patent specifications for the benefit of the public in exchange for the right to exclude others from practicing the invention for the duration of the patent's term.[8]

II. Evaluate Whether The Application Complies With the "Written Description" Requirement

The inquiry into whether the description requirement is met must be determined on a case-by-case basis and is a question of fact.[9] The examiner has the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims.[10] Office personnel should adhere to the following procedures when reviewing patent applications for compliance with the written description requirement of 35 U.S.C. 112, ¶ 1.

A. Review the Entire Application To Determine What Applicant has Invented, the Field of the Invention and the Level of Predictability in the Art

Prior to determining whether the claims satisfy the written description requirement, Office personnel should review the entire specification, including the specific embodiments, figures, sequence listings, and the claims, to understand what applicant has invented and the correspondence between what applicant has described, i.e., has possession of, and what applicant is claiming. Such a review should be conducted from the standpoint of one of skill in the art at the time the application was filed and should include a determination of the field of the invention and, thus, the level of predictability in the art. Predictability of the structure of a species can be premised upon:

(1) Whether the level of skill in the art leads to a predictability of structure; and/or

(2) Whether teachings in the application or prior art lead to a predictability of structure.

There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function. Thus, in some factual situations, the written description requirement may be satisfied through disclosure of function alone when there is a well-established correlation between structure and function. In contrast, without such a correlation, prediction of structure from function is highly unlikely. In this latter case, disclosure of function alone will not satisfy the written description requirement.[11]

B. For Each Claim, Determine What the Claim as a Whole Covers

Each claim must be separately analyzed and given its broadest reasonable interpretation.[12] The entire claim, including its preamble language and transitional phrase, must be considered. "Preamble language" is that language in a claim appearing before a transitional phase, e.g., before "comprising," "consisting essentially of," or "consisting of". The transitional term "comprising" (and other comparable terms, e.g., "containing" and "including") is "open-ended"—it covers the expressly recited subject matter alone or in combination with other unstated subject matter.[13] There must be adequate written description to support the claimed invention *including* the preamble.[14] The claim as a whole, including all limitations found in the preamble, the transitional phrase, and the body of the claim, must be described sufficiently to satisfy the written description requirement.[15] For claims of the form "A.[structure] comprising SEQ ID NO: 1" there may be a written description problem if the claim as a whole, including its preamble and transitional phrase, is directed to an invention of unpredictable structure that is not fully described.

For example, when the term "gene," "mRNA," or "cDNA" is recited in the preamble, it implies a specific structure (or a small genus of specific structures) when used in the traditional sense, i.e., to mean the structure having the naturally occurring sequence. Thus, "A gene comprising SEQ ID NO: 1"; "A mRNA comprising SEQ ID NO: 1"; and "A cDNA comprising SEQ ID NO: 1" implicitly recite specific structures such as promoters, enhancers, coding regions, and other regulatory elements in the preamble which must be sufficiently described in the specification so as to show the applicant was in possession of the claimed inventions.

In contrast, use of less specific, generic preamble language, such as "composition," "nucleic acid," "DNA," and "RNA," does not typically present a written description problem. These terms are sufficiently general that one skilled in the art can readily envision a sufficient number of members of the claimed genus to provide written description support for the genus.

A claim such as "A gene comprising SEQ ID NO: 1," can be viewed as a species claim in which the preamble recites a combination and the body of the claim recites a subcombination: The "gene" is the combination and "SEQ ID

NO: 1" (which is a fragment of the gene) is the subcombination. Written description of only the subcombination (in this example the fragment SEQ ID NO: 1) normally does not put one in possession of the combination (in this example the gene).

Likewise, generic claims to sequences can be viewed as a genus of such combination-subcombination claims. For example, a claim such as "A nucleic acid comprising SEQ ID NO: 1" can be viewed as a genus claim in which each member of the genus (each species) is itself a combination-subcombination: Each member of the genus "nucleic acid" is a combination containing the subcombination "SEQ ID NO: 1" (which is a fragment of the nucleic acid). Again, the generic term "nucleic acid" does not typically present a written description problem because one skilled in the art can readily envision a sufficient number of members of the claimed genus to provide written description support for the genus. [16]

C. For Each Claimed Species, Determine Whether There is Sufficient Written Description To Inform a Skilled Artisan That Applicant was in Possession of the Claimed Invention at the Time the Application was Filed

Written description may be satisfied through disclosure of relevant identifying characteristics, i.e., structure, other physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is well known to one skilled in the art need not be disclosed. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.

For each claimed species:

(1) Determine whether a complete structure is disclosed. The complete structure of a species typically satisfies the requirement that the description be set forth in "such full, clear, concise and exact terms" to show possession of the claimed invention. If a complete structure is disclosed, the written description requirement is satisfied for that species, and a rejection under 35 U.S.C. 112 ¶ 1 for lack of written description must not be made.

For example, consider the following claim:

A probe for use in detecting nucleic acid sequences coding for enzyme Q from the genus Bacillus consisting of SEQ ID NO: 16.

Considering the claim as a whole, it is a species claim covering the probe SEQ ID NO: 16. The specification discloses the complete sequence for SEQ ID NO: 16. Thus, this claim falls into the "safe harbor" described under C(1).

(2) If the complete structure is not disclosed, determine whether the specification discloses other relevant identifying characteristics, i.e., physical and/or chemical characteristics and/or functional characteristics coupled with a known or disclosed correlation between function and structure, sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. Disclosure of any combination of such identifying characteristics that would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. In such a case, a rejection for lack of written description under 35 U.S.C. 112 ¶ 1 must not be made.

For example, consider the following claim:

An isolated double-stranded DNA consisting of (1) a single-stranded DNA which has a molecular size of 2.57 Kb and is derived from golden mosaic virus, and (2) a DNA complementary to said single-stranded DNA, giving the restriction endonuclease cleavage map shown in FIG.2(a) and having no Mbo I restriction endonuclease site.

Although the specification does not disclose the complete structure for the claimed DNA, it does disclose sufficient identifying characteristics, i.e., size, cleavage map, and source from which the DNA is derived. Thus, while this claim does not meet the C(1) criteria because the complete sequence is not disclosed, it does meet the C(2) criteria because one skilled in the art would recognize from the characteristics, e.g., size, map, source, that applicant was in possession of the claimed material at the time of filing.

The following protein claim also falls within the C(2) criteria:

An isolated alginate lyase enzyme wherein said enzyme lyses alginate in the mucous substance produced in a patient with cystic fibrosis and wherein said enzyme has the N-terminal amino acid sequence SEQ ID No. 1, obtained from Flavobacterium pepermentium and has the following physicochemical properties: (1) Activity: lyses alginate to saccharides having a non-reducing end C_4–C_5 double bond and ultimately to 4-deoxy-5-ketouronic acid; (2) Molecular weight: 60,000 daltons; (3) Optimal pH: 8.0; (4) Stable pH: 6.0–8.0; (5) Optimal temperature: 70 degrees C; and (6) Substrate specificity: alginate.

In this example, the specification discloses the molecular weight, origin, activity, and specificity but does not disclose the complete structure for the claimed enzyme. Thus, this claim would not meet the C(1) criteria because the complete sequence is not disclosed. However, the claim meets the C(2) criteria because, although the complete structure is not disclosed, one skilled in the art would recognize from the disclosed physical characteristics—e.g., molecular weight, origin, activity, and specificity—that applicant was in possession of the claimed material at the time of filing.

In contrast, consider the following claim:

An isolated nucleotide sequence consisting of the sequence of the reverse transcript of a human mRNA, which mRNA encodes insulin.

The specification in this example provides the coding sequence for rat insulin but not that for human insulin. The description for the reverse transcript of human mRNA is limited to its function, encoding human insulin, and to a method for isolating the claimed sequence from its natural source. A sequence described only by a *purely* functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed species. In this case, even though a genetic code table would correlate a known insulin amino acid sequence with a genus of coding nucleic acids, the same table cannot predict the native, naturally occurring nucleic acid sequence of human mRNA or its corresponding cDNA. Thus, the specification in this example does not provide adequate written description, either under the C(1) or C(2) criteria.

Any claim to a species that does not meet the test described under C(1) or C(2)must be rejected as lacking adequate written description under 35 U.S.C. 112 ¶ 1.

D. For Each Claimed Genus, Determine Whether There is Sufficient Written Description to Inform a Skilled Artisan That Applicant was in Possession of the Claimed Genus at the Time the Application was Filed

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by relevant identifying characteristics, i.e., structure or other physical and/or chemical characteristics, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" requires that the species which are expressly described be representative of the entire genus. Thus, when there is substantial variation within the genus, it may require a description of the various species which reflect the variation within the genus. For example, a broadly drawn claim to a specific gene from ruminant mammals may require a representative species from cattle, buffalo, bison, goat, deer, antelope, camel, giraffe and llama.

What constitutes a "representative number" is an inverse function of the predictability of the art, as determined in IIA above. The number must be sufficient to reasonably identify the other members of genus. In an unpredictable art, adequate written description of a genus *cannot* be achieved by disclosing only one species within the genus. In fact, if the members of the genus are expected to vary widely in their identifying characteristics, such as structure and activity, written description for each member within the genus may be necessary.

Generalized descriptions alone, such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," fail to satisfy the written description requirement because they do not describe any members of the genus except by function without any known or disclosed correlation between function and structure.[24] If the correlation between structure and function in the art would not have been known to one skilled in the art and the specification does not describe the correlation, the written descriptive support cannot depend on that correlation.

For each claim to a genus:

(1) Determine whether a representative number of species have been described by complete structure as in C(1) above. If a representative number have been so described, then the applicant has written description support for the claimed genus and a rejection under 112 ¶ 1 for lack of written description must not be made.

For example, consider the following claim to a genus:

> An isolated DNA probe for detecting HIV-X, wherein said DNA probe hybridizes to the nucleotide sequence set forth in SEQ ID NO:1 under the following conditions: hybridization in 7% sodium dodecyl sulfate (SDS), 0.5M $NaPO_4$ pH 7.0, 1mM EDTA at 50° C.; and washing with 1% SDS at 42° C.

In this case, the specification discloses the sequence of the isolated DNA molecule consisting of SEQ ID NO: 1 and discloses several sequences that hybridize to SEQ ID NO: 1. Hybridization under the stringent conditions specified here requires that the claimed nucleic acid probes be structurally similar to the complement of the nucleic acid sequence disclosed as SEQ ID NO: 1. In this case, the description as a whole is sufficient to evidence possession of the claimed genus because the genus is defined by relation to the structure of the sequence provided as SEQ ID NO: 1, and because several species are disclosed that possess the hybridization property which further defines the genus. Thus, this claim to a genus meets the D(1) criteria.

(2) For each claim to a genus not supported as described under D(1), determine whether there is a representative number of adequately described species, as analyzed under C(2). The representative number must permit one skilled in the art to reasonably identify the remaining members of the genus. If a representative number are so described, then the written description requirement is satisfied and, again, a rejection under 112 ¶ 1 for lack of written description must not be made.

For example, consider the following claim to a genus:

> A monoclonal antibody which specifically binds to the novel cancer associated TAG-31 antigen but which does not substantially bind normal adult human tissues, wherein said monoclonal antibody has a binding affinity of greater than 3 times 10^9 M^{-1} for TAG-31.

Considering the claim as a whole, it is drawn to a genus of monoclonal antibodies. Although the specification does not disclose the complete structure of a representative number of species to support the claimed genus of antibodies, it does disclose multiple monoclonal antibodies which have the isotype claimed as well as the binding specificity and binding affinity characteristics recited in the claims. In this well-developed art, additional identifying characteristics for a substantial portion of the genus are well-known (e.g., number of chains, disulfide bonds, constant and variable regions, etc.). Thus, applicant's disclosure combined with what was known in the art are sufficient to describe the claimed genus of monoclonal antibodies in such full, clear, concise and exact terms to show applicant was in possession of the claimed antibodies. Thus, the claim meets the D(2) criteria.

As another example, consider the following claim to a genus:

> An isolated mutanase enzyme produced by Bacillus having the following physicochemical properties (1) to (9): (1) action: an ability to cleave alpha-1,3-glucosidic links of mutan; (2) substrate specificity: an ability to effectively decompose mutan; (3) optimum pH: pH 4 to 4.5 when reacting on a mutan substrate at 35 degrees C for 10 minutes; (4) pH range for stability: pH 4 to 10 when kept at 25 degrees C for 24 hours; (5) optimum temperature: 50 degrees to 65 degrees C when reacted at pH 5 with mutan as a substrate; (6) thermal stability: enzyme activity remains stable below 50 degrees C after incubation at pH 5 for 10 minutes; (7) effect of metal ions: mercury and silver show inhibitory effect on a mutan substrate; (8) effect of inhibitors: p-chloromercurybenzoic acid shows inhibitory effect on a mutan substrate; and (9) molecular weight: about 140,000 to about 160,000 as determined by SDS-polyacrylamide gel electrophoresis.

Considering the claim as a whole, it covers a genus of mutanase enzymes. Although the specification does not disclose the complete structure of a representative number of species to support the claimed genus of enzyme compositions, it does disclose 3 mutanase species produced by different strains of Bacillus (mutanases A, B and C) which are identified by multiple relevant identifying characteristics, i.e., molecular weight, substrate specificity, optimum and ranges of temperature and pH for mutan cleavage activity, etc. In this well-developed art, these identifying characteristics are sufficient for a skilled artisan to recognize applicant had possession of the species from the identifying characteristics of the three mutanase species, to reasonably predict sufficient identifying characteristics of the other members of the genus and, thus, establish possession of the genus. Thus, the claim meets the D(2) criteria.

As another example, consider the following claim to a genus:

A DNA comprising a novel DF3 enhancer and DNA encoding a heterologous gene but not encoding DF3 wherein said DF3 enhancer consists of SEQ ID NO: 1.

Considering the claim as a whole, it covers a genus of DNA. The specification does not describe a representative number of members of the genus by complete structure. Thus, the claim does not meet the D(1) criteria. However, there is sufficient disclosure of identifying characteristics common to the members of the genus, i.e., DF3 enhancer, to meet the D(2) criteria. Because of the nature of the generic term "DNA," one skilled in the art could envision a sufficient number of the members of the genus to describe the invention in such full, clear and concise terms as to show possession of the invention at the time of filing.

In contrast, consider the claim:

An isolated nucleic acid comprising the structure of the reverse transcript of a mammalian mRNA, which mRNA encodes insulin.

Considering the claim as a whole, the claim covers the genus of nucleotide sequences encoding mammalian insulin. The specification only provides the coding sequence for rat insulin cDNA and a method to isolate the coding sequence from its natural source.[25] This description does not meet the criteria of D(1) or D(2) and thus does not satisfy the written description requirement.

Also contrast the claim "A gene comprising SEQ ID NO: 1." Although all genes encompassed by this claim share the characteristic of comprising SEQ ID NO: 1, and as such might appear to meet the D(2) criteria, there is insufficient description of the characteristics (e.g., promoters, enhancers, coding regions, and other regulatory elements) which identify the genes, as opposed to any DNA comprising SEQ ID NO: 1.

If sufficient identifying characteristics are not disclosed for a given genus, as described in D(1) or D(2), the claim to that genus must be rejected as lacking adequate written description under 35 U.S.C. 112 ¶ 1.

III. Complete Patentability Determination Under All Statutory Requirements and Clearly Communicate Findings, Conclusions and Their Bases

The above only describes how to determine whether the written description requirement of 35 U.S.C. 112 ¶ 1 is satisfied. Regardless of the outcome of that determination, Office personnel must complete the patentability determination under all the relevant statutory provisions of the Patent Act.

Once Office personnel have concluded analysis of the claimed invention under all the statutory provisions, including 35 U.S.C. 101, 112, 102 and 103, they should review all the proposed rejections and their bases to confirm their correctness. Only then should any rejection be imposed in an Office action. The Office action should clearly communicate the findings, conclusions and reasons which support them.

Specific to these guidelines:

A. For Each Claim Lacking Written Description Support, Reject the Claim Under Section 112, ¶ 1, for Lack of Adequate Written Description

In rejecting a claim, set forth express findings of fact regarding the above analysis which support the lack of written description conclusion. These findings should:

(1) identify the claim limitation not described; and

(2) provide reasons why a person skilled in the art at the time the application was filed would not have recognized the description of this limitation in view of the disclosure of the application as filed.

When appropriate, suggest amendments to the claims which would bring the claims into compliance with the written description in the specification, bearing in mind the prohibition against new matter in the claims and corresponding description set forth in 35 U.S.C. 112 and 132.

B. Upon Reply by Applicant, Again Determine the Patentability of the Claimed Invention, Including Whether the Written Description Requirement is Satisfied by Performing the Analysis Described Above in View of the Whole Record

Upon reply by applicant, before repeating any rejection under Section 112 ¶ 1 for lack of written descriptive basis, review the basis for the rejection in view of the record as a whole, including amendments, arguments and any evidence submitted by applicant. If the whole record now demonstrates that the written description requirement is satisfied, do *not* repeat the rejection in the next Office action. If the record still does not demonstrate that written description is adequate to support the claim(s), repeat the rejection under 35 U.S.C. 112 ¶ 1, fully respond to applicant's rebuttal arguments, and properly treat any further showings submitted by applicant in the reply. Any affidavits, including those relevant to the 112 ¶ 1 written description requirement, must be thoroughly analyzed and discussed in the Office action.

Endnotes

1. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).
2. 984 F.2d 1164, 25 USPQ2d 1601 (Fed. Cir. 1993).
3. 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991).
4. *E.g., Vas-Cath, Inc.* v. *Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).
5. *In re Barker*, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977).
6. 35 U.S.C. §§ 132 & 251.
7. *E.g., Vas-Cath, Inc.* v. *Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Much of the written description case law addresses whether the specification as originally filed supports claims not originally in the application. The issue raised in the cases is most often phrased as whether the original application provides "adequate support" for the claims at issue or whether the material added to the specification incorporates "new matter" in violation of 35 U.S.C. § 132. The "written description" question similarly arises in the interference context, where the issue is whether the specification of one party to the interference can support the newly added claims corresponding to the count at issue, i.e., whether that party can "make the claim" corresponding to the interference count. *E.g., see Martin* v. *Mayer*, 823 F.2d 500, 502, 3 USPQ2d 1333, 1335 (Fed. Cir. 1987).

In addition, early opinions suggest the Patent and Trademark Office was unwilling to find written descriptive support when the only description was found in the claims; however, this viewpoint was rejected. *See In re Koller*, 613 F.2d 819, 204 USPQ 702 (CCPA 1980) (original claims constitute their own description); *In re Gardner*, 475 F.2d 1389, 177 USPQ 396 (CCPA 1973) (accord); *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976) (accord). It is now well-accepted that a satisfactory description can be mined from the claims or any other portion of the originally filed specification.

These early opinions did not address the quality or specificity of particularity that was required in the description, i.e., how much description is enough.

8. *See Eli Lilly*, 119 F.3d at 1566, 43 USPQ2d at 1404.
9. *See In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) ("Precisely how close [to the claimed invention] the description must come to comply with § 112 must be left to a case-by-case development."); *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976) (inquiry is primarily factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure).
10. *Wertheim*, 541 F.2d at 262, 191 USPQ at 96.
11. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 (written description requirement not satisfied by merely providing "a result that one might achieve if one made that invention"); *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372–73

(Fed. Cir. 1984) (affirming a rejection for lack of written description because the specification does "little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate").

12. *See, e.g., In re Morris*, 127 F.3d 1048, 1053–54, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997).

13. *See, e.g., Ex parte Davis*, 80 USPQ 448, 450 (1948) ("comprising" leaves the "claim open for the inclusion of unspecified ingredients even in major amounts".), *quoted with approval in Moleculon Research Corp* v. *CBS, Inc.*, 793 F.2d 1261, 1271, 229 USPQ 805, 812 (Fed. Cir. 1986).

14. *See Pac-Tec Inc.* v. *Amerace Corp.*, 903 F.2d 796, 801, 14 USPQ2d 1871, 1876 (Fed. Cir. 1990) (determining that preamble language that constitutes a structural limitation is actually part of the claimed invention).

15. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. *Lockwood* v. *American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

16. *E.g., Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1405–06.

17. A "relevant identifying characteristic" is one that would provide evidence that applicant was in possession of what is claimed. For example, the presence of a restriction enzyme map of a gene may be relevant to a statement that the gene has been isolated. One skilled in the art could determine whether the gene disclosed was the same as or different than a gene isolated by another by comparing the restriction enzyme map. In contrast, evidence that the gene could be digested with a nuclease would not normally represent a relevant characteristic since any gene would be digested with a nuclease.

Examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics can demonstrate the requisite possession. For example, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross reactivity may be sufficient to show possession of the claimed invention to one of skill in the art. *See Lockwood* v. *American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997) ("written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams, formulas, etc. that fully set forth the claimed invention").

However, a definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. *See also Fiers*, 984 F.2d at 1169–71, 25 USPQ2d at 1605–06 (discussing Amgen).

18. *See Hybritech Inc.* v. *Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379–80, 231 USPQ 81, 90 (Fed. Cir. 1986).

19. *See, e.g., Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin* v. *Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in ipsis verbis to be sufficient").

20. 35 U.S.C. § 112 ¶ 1. *Cf. Fields* v. *Conover*, 443 F.2d 1386, 1392, 170 USPQ 276, 280 (CCPA 1971) (finding a lack of written description because the specification lacked the "full, clear, concise, and exact written description" which is necessary to support the claimed invention).

21. The examples contained within these guidelines are not intended to represent the minimum requirements necessary to comply with 35 U.S.C. § 112 ¶ 1.

22. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

23. *See id.* at 1568, 43 USPQ2d at 1406.

24. *Cf. Eli Lilly*, 119 F.3d at 1567, 43 USPQ2d at 1405 (stating that "The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning itself.").

25. *See id.* 1568, 43 USPQ2d at 1406.

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